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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,145	STEELE ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8,67,75,82-88 and 91-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,67,75,82-88 and 91-97* is/are rejected.

7)☒ Claim(s) *7 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-33, 67-73, 75-80 and 82-88, and SEQ ID NO:64, in the reply filed on May 24, 2004 is acknowledged.

Claims 2-6, 9-66, 68-74, 76-81 and 89-90 are cancelled.

Claims 1, 67, 75 and 82 are currently amended.

Claims 91-97 are newly added.

Claims 1, 7-8, 67, 75, 82-88 and 91-97 are pending and are examined.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, filed December 19, 2001, is attached to the instant Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 67, 75, 82-88 and 91-97 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid molecule that encodes a (-)-camphene synthase and that hybridizes to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 3 X SSC at 65°C for 16 hours followed by one wash in 0.5 X SSC at 55°C for 30 minutes, including an isolated nucleic acid molecule wherein the isolated nucleic acid molecule hybridizes to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 5 X SSC at 65°C for 16 hours followed by two washes in 0.2 X SSC at 65°C for 20 minutes per wash. The claims are also drawn to a replicable expression vector comprising said nucleic acid molecule, a host cell comprising said vector, and a method of enhancing the production of a (-)-camphene synthase in a suitable host cell comprising introducing into the host cell said expression vector under conditions enabling expression of the (-)-camphene synthase in the host cell.

The specification describes the elected sequence of SEQ ID NO:64 as a 2013 base pair cDNA sequence obtained from mRNA isolated from wounded grand fir (*Abies grandis*) sapling stems, said cDNA having a 1854 base pair ORF encoding the 618 amino acids of SEQ ID NO:65 (page 56; sequence listing). The specification also describes SEQ ID NO:65 as being in the gymnosperm Tpsd subfamily of plant terpenoid synthases, and as being most closely related to grand fir monoterpene synthases. The specification additionally describes SEQ ID NO:65 as encoding a preprotein bearing an amino-terminal transit peptide for plastidal import. (page 56). The specification further describes a recombinant truncated form of SEQ ID NO:65 as exhibiting (-)-camphene synthase activity (page 61). The specification describes SEQ ID NO:3 as a 2018 base pair cDNA

sequence obtained from mRNA isolated from wounded grand fir (*Abies grandis*) sapling stems, said cDNA having a 1884 base pair ORF encoding the 628 amino acids of SEQ ID NO:4 (page 41; sequence listing). The specification also describes SEQ ID NO:4 as encoding a preprotein bearing an amino-terminal transit peptide for plastidal import. (page 41). The specification additionally describes a recombinant form of SEQ ID NO:4 as exhibiting (-)-pinene synthase activity (pages 42-46).

The specification does not describe SEQ ID NO:3 as encoding a polypeptide that has (-)-camphene synthase activity, or describe a correlation between (-)-camphene synthase activity and the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694. The specification also does not describe any sequence other than the elected sequence of SEQ ID NO:64 that encodes a polypeptide that has (-)-camphene synthase activity. The specification additionally discloses that cDNAs encoding polypeptides having (-)-camphene synthase activity have not been described previously from any source (page 63).

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

In the instant case Applicant has not described a representative number of species falling within the scope of the claimed genus which encompasses multiple sequences

from undisclosed sources that hybridize under defined conditions to a defined portion of SEQ ID NO:3 and that encode a (-)-camphene synthase, nor the structural features unique to the genus, as Applicant has described only a single sequence encoding a (-)-camphene synthase, and other (-)-camphene synthase coding sequences are not known or disclosed.

Claims 1, 67, 75, 82-88 and 91-97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO:65, a vector comprising said nucleic acid, a prokaryotic or plant host cell comprising said vector, and a method for enhancing the production of a (-)-camphene synthase of SEQ ID NO:65 in prokaryotic or plant host cell, does not reasonably provide enablement for other isolated nucleic acids encoding a (-)-camphene synthase, or for any unspecified eukaryotic host cell comprising a vector comprising a nucleic acid encoding a (-)-camphene synthase , or for a method for enhancing the production of a (-)-camphene synthase in any unspecified eukaryotic host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to an isolated nucleic acid molecule that encodes a (-)-camphene synthase and that hybridizes to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 3 X SSC at 65°C for 16 hours followed by one wash in 0.5 X SSC at 55°C for 30 minutes, including an isolated nucleic acid molecule wherein the isolated nucleic acid molecule hybridizes to the complement of the portion of SEQ ID NO:3 extending from nucleotide

1560 to nucleotide 1694 under hybridization conditions of 5 X SSC at 65°C for 16 hours followed by two washes in 0.2 X SSC at 65°C for 20 minutes per wash. The claims are also drawn to a replicable expression vector comprising said nucleic acid molecule, a host cell comprising said vector, including a prokaryotic host cell, a eukaryotic host cell and a plant host cell, and a method of enhancing the production of a (-)-camphene synthase in a suitable host cell, including a prokaryotic host cell, a eukaryotic host cell and a plant host cell, comprising introducing into the host cell said expression vector under conditions enabling expression of the (-)-camphene synthase in the host cell.

The specification discloses that the elected sequence of SEQ ID NO:64 is a 2013 base pair cDNA sequence obtained from mRNA isolated from wounded grand fir (*Abies grandis*) sapling stems encoding the 618 amino acids of SEQ ID NO:65 (page 56; sequence listing). The specification also discloses the expression of full-length and truncated forms of SEQ ID NO:65 in *E. coli* host cells, and that the truncated form of SEQ ID NO:65 exhibits detectable (-)-camphene synthase activity (pages 60- 61). The specification discloses that SEQ ID NO:3 is a 2018 base pair cDNA sequence obtained from mRNA isolated from wounded grand fir (*Abies grandis*) sapling stems encoding the 628 amino acids of SEQ ID NO:4 (page 41; sequence listing). The specification additionally discloses that a recombinant form of SEQ ID NO:4 exhibits (-)-pinene synthase activity (pages 42-46).

The specification does not disclose that SEQ ID NO:3 encodes a polypeptide that has (-)-camphene synthase activity, or that (-)-camphene synthase activity is correlated with the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694. The specification also does not disclose any sequence other than the elected sequence of

SEQ ID NO:64 that encodes a polypeptide that has (-)-camphene synthase activity. The specification further discloses that cDNAs encoding polypeptides having (-)-camphene synthase activity have not been described previously from any source (page 63).The specification additionally does not disclose eukaryotic host cells comprising a vector comprising a nucleic acid encoding a (-)-camphene synthase, or the enhancement of the production of a (-)-camphene synthase therein.

The full scope of the claimed invention is not enabled because the specification does not provide sufficient guidance with respect to where and how to obtain isolated nucleic acid molecules that encode a (-)-camphene synthase and that hybridize to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 3 X SSC at 65°C for 16 hours followed by one wash in 0.5 X SSC at 55°C for 30 minutes.

Such guidance is necessary because one cannot predictably obtain nucleic acid molecules that encode a (-)-camphene synthase solely on the basis of their hybridizing to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694, since the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 is not know or disclosed as being correlated with (-)-camphene synthase activity. One also cannot predictably obtain nucleic acid molecules that encode a (-)-camphene synthase from any unspecified source, as monoterpene synthases such as a (-)-camphene synthase enzymes appear to be unique to certain members of the plant kingdom. See, for example, Bohlmann et al., (Proc. Natl. Acad. Sci. USA, Vol. 95, pages 4126-4133, April 1998), who describe monoterpene synthases as being of plant origin.

Absent guidance with respect to where and how to obtain the claimed isolated nucleic acid molecules that encode a (-)-camphene synthase, one skilled in the art would have one skilled in the art would have to first identify and clone from undisclosed sources nucleic acids that meet the structural limitations of the claims, and then test by trial and error the enzymatic activity of the protein encoded by each nucleic acid so obtained in order to discriminate between those nucleic acids that encode (-)-camphene synthases and those that do not. Such trial and error testing of sequences identified and cloned from undisclosed sources would constitute undue experimentation.

The full scope of the claimed invention is also not enabled because the effect of expressing a nucleic acid encoding a (-)-camphene synthase in any unspecified eukaryotic cell is unpredictable, since monoterpenes such as camphene that would be produced as a consequence of (-)-camphene synthase expression are known to be toxic to certain types of eukaryotic cells. See, for example, Bohlmann et al., who teach that monoterpenes produced by plants such as the grand fir are known in the art to be toxic to insects and their fungal symbionts (Archives of Biochemistry and Biophysics, 1999, Vol. 368, No. 2, pages 232-243, see page 233). See also the specification at page 2 which teaches that the volatile fraction of monoterpene-containing conifer oleoresin is known in the art to be toxic to both bark beetles and their fungal associates (lines 7-13).

Absent guidance with respect to the type of eukaryotic host cell in which to express an isolated nucleic acid molecule encoding a (-)-camphene synthase, one skilled in the art would have to test by trial and error the effect of expressing such nucleic acids in the various different types of eukaryotic host cell systems available (mammalian, fungal, insect, etc.) in order to discriminate between those host cell systems in which (-)-

camphene synthase production would be enhanced upon its expression and those that would not. Such trial and error testing of the effect of expressing nucleic acid molecules encoding (-)-camphene synthases in undisclosed host cell systems would constitute undue experimentation.

Allowable Subject Matter

Claims 7 and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

Remarks

Claims 7 and 8 are objected to.

Claims 1, 67, 75, 82-88 and 91-97 are rejected.

The claims are deemed free of the prior art, due to the failure of the prior art to teach or suggest an isolated nucleic acid encoding SEQ ID NO: 65, or an isolated nucleic acid molecule that encodes a (-)-camphene synthase and that hybridizes to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 3 X SSC at 65°C for 16 hours followed by one wash in 0.5 X SSC at 55°C for 30 minutes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins Cynthia Collins 8/6/04